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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,090	01/22/2007	Yechezkel Barenholz	BARENHOLZ17	4718

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,090	BARENHOLZ ET AL.	
	Examiner	Art Unit	
	GOLLAMUDI S. KISHORE	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I in the reply filed on 5-17-10 is acknowledged.

Claims included in the prosecution are 62-75.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of inflammation, does not reasonably provide enablement for treatment or prevention of diseases or disorder of mucosa. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those in the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is

the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: the invention concerns with treatment or prevention of a disease or disorder of the mucosa using anionic liposomes containing a medicament (claim 62). The diseases include ulcerative colitis, Crohn's disease, irritable bowel syndrome, colon carcinoma and familial adenomatous polyposis (claims 69 and 75).

2) The state of the prior art: the state of the prior art is very high in terms of formulating the liposomal sustained release compositions and treating specific diseases using specific drugs and specific cancers using specific anti-cancer agents.

3) The relative skill of those in the art: the skill of one of ordinary skill in the art is very high (Ph.D level technology).

4) The predictability or unpredictability in the art: It should be pointed out that the independent claim does not even recite a specific drug and the dependent claim recite drugs in generic terms and no specific anti-cancer drugs are recited although the dependent claims recite most drugs in generic terms and it is unclear which of these drugs treat which of the claimed diseases. With regard to colon carcinoma, the examiner cites Trosko (Mutation Research, 2001) as interest which shows that our current conventional approaches of cancer prevention/therapy have had limited success and in some cases such as treatment for pancreatic cancer, it has been a total failure. Trosko further teaches that we now know each organ specific tumor expresses different genes and furthermore, within a given tissue, no two tumors are genetically/phenotypically alike, it would be extremely naive to believe t hat all tumors

could be treated with some sort of a single therapy. According to Trosko, each phase of complex carcinogenic process represents cells at different genotypic/phenotypic stages and in addition, cancers are characterized by genetic instability and the excessive cell proliferation that give rise to cancers by multiple mechanisms through multiple pathways.

5). the breadth of the claims: instant claim is very broad in terms of diseases to be treated.

6) The amount of direction of guidance provided: instant specification does not provide adequate guidance in terms of the diseases claimed and the various active agents claimed.

7) The presence or absence of working examples: no working examples are provided for the effectiveness of anionic liposomes against the various diseases claimed.

8) The quantity of experimentation necessary: since as pointed out above, the generic term encompasses various diseases including colon carcinoma and one cannot determine the effectiveness of the claimed composition without undue experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 62-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The meets and bounds of ‘active ingredient and ‘disease or disorder of the mucosa’ n claim 62 are unclear. The dependent claim 69 for example recites nausea and reflux. It is unclear how these are mucosal diseases or conditions.

What is being conveyed by Mesalamine (5ASA) and ‘Probiotics g. cyclosporin A’ in claim 72? The meets and bounds of derivatives of 5-aminosalicylic acid are unclear.

'or’ is missing between ‘long term oxidative stress’ and ‘short term oxidative stress’ in claim 68.

The meets and bounds of ‘SOD mimics’ and ‘therapeutic reducing agents’ in claim 74 are unclear.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 74 recites the

broad recitation free radical scavengers, and the claim also recites tocopherol, SOD, SOD mimics and catalase which are the narrower statements of the range/limitation.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 62-66 and 68-75 are rejected under 35 U.S.C. 102(a) as being anticipated by Qi (US 2003/0095999).

Instant claim 62 recites the treatment of a disease or disorder of the mucosa by administering negatively charged liposomes loaded with active ingredients. Among the conditions recited are nausea, inflammation and colon carcinoma. Similarly instant claim 76 recites the prevention of a disease or condition of the mucosa

Qi teaches anionic liposomal compositions for the delivery of active agents within and/or beneath the mucosal membranes. The drugs encapsulated within the anionic liposomes include antibiotics, steroids, non-steroidal anti-inflammatory drugs such as prednisone, antiemetics, chemotherapeutic agents and vitamins (0023, 0038, 0039, 0049, 0081-0083, 0096, 0099-0102, 0126, 0145-0149). Since Qi teaches that the anionic liposomes deliver the active agents within the mucosa of the host treatment and prevention of the conditions such as inflammation, nausea and carcinoma are implicit in the teachings of Qi. Qi teaches vitamins which include antioxidant vitamins such as

vitamin E and therefore, treatment of conditions relating to oxidative stress is implicit in Qi.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 62-65 and 68-75 rejected under 35 U.S.C. 103(a) as being unpatentable over Qi cited above.

The teachings of Qi have been discussed above. Qi does not teach the treatment of all the diseases claimed through examples. However, in view of the suggestion of various active agents which could be incorporated and the guidance provided by Qi, it would have been obvious to one of ordinary skill in the art to prepare various compositions for the treatment of various diseases with a reasonable expectation of success.

9. Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qi cited above in combination with Iga (5,080,904) or Fossheim (US 2004/0170560, or Dyvik (US 2002/0039556) or Schneider (6,258,378) individually or in combination.

The teachings of Qi have been discussed above. Qi teaches the use of phosphatidylserine to form the anionic liposomes. Qi does not teach the use of phosphatidylglycerol or a saturated form of phosphatidylglycerol. The use of DSPG

instead of phosphatidylserine taught by Qi would have been obvious to one of ordinary skill in the art since Iga, Fossheim, Dyvik and Schneider teach that for the preparation of liposomes either phosphatidylserine or phosphatidylglycerol could be used (see lines 35-56 of Iga; 0029 of Fossheim; 0031 of Dyvik and col. 4, lines 41-48 of Schneider).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GOLLAMUDI S. KISHORE whose telephone number is (571)272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612

GSK